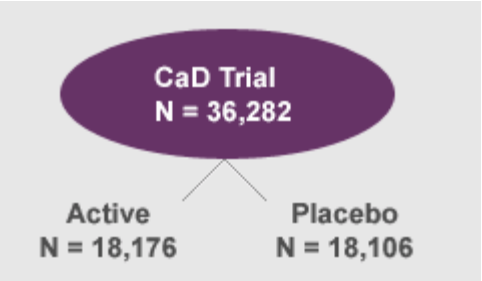
WHI Calcium and Vitamin D Trial Overview

Background



Previous research on dietary or supplemental calcium have suggested that increased intake is associated with a decreased risk of osteoporosis and increased bone density. Vitamin D is often added to calcium to increase its absorption in the body. The effects of calcium and vitamin D on actual fracture incidence, however, had not been determined. The WHI Calcium and Vitamin D Trial (CaD) was designed to test the effects of calcium and vitamin D supplementation on women's risk for hip fractures (primary analyses) and other fractures and colorectal cancer (secondary analyses). Previous research on calcium and vitamin D and disease outcomes, as background to the WHI CaD trial, are reviewed in the WHI Protocol.

Screening and Eligibility

Participants randomized to the WHI Clinical Trial (HT or DM) were eligible for the CaD Trial 12 to 24 months after randomization. Eligibility criteria for CaD were focused on safety (e.g., no previous hypercalcemia or renal calculi), and competing risk (e.g., no medical condition associated with survival of less than three years). Participants were eligible for CaD even if they were taking their own supplemental calcium or vitamin D, although their personal use of vitamin D had to be 600 IU or less, for safety reasons. A total of 36,282 CT participants were also randomized to CaD

Intervention

Participants in CaD were randomized in a 1:1 fashion to one of two arms:

- Calcium carbonate with 1000 mg of elemental calcium combined with vitamin D3 400 IU per day, taken in two divided doses daily
- Placebo, taken as one pill twice a day

CaD study pills were initially available in a chewable (peppermint-flavored) format only. Because some participants did not tolerate this formulation well (e.g., didn't like the taste or texture), an optional swallow-able formulation was developed and offered, starting in July 1997, to eligible participants (who were offered a visual inspection and/or "taste test") before randomization and to all randomized CaD participants during follow-up visits. Participants were told that they could switch between the chewable and swallow-able formulations at any contact during which new study pills were dispensed.

At randomization all CaD participants were given a "CaD Information Sheet" (which was revised to a more detailed "CaD Handbook" in late 2002). This participant material was offered each time study pills were dispensed and included trial-specific information about:

- Safety (e.g., notifying staff if high blood calcium or bladder or kidney stones are diagnosed)
- Adherence (e.g., taking study pills daily, managing symptoms)
- Retention (e.g., coming in for clinic visits)

Follow-up

Data Collection

CaD participants were contacted by phone 4 weeks after randomization to complete a management (e.g., symptoms, adherence, and pill tolerance) and safety interview, which was repeated semi-annually thereafter while the participant was taking study pills. CaD participants, otherwise, had routine contacts based on their Clinical Trial (CT) follow-up schedule.

If symptom or safety concerns (e.g., constipation, renal calculi) or adherence challenges (e.g., difficulty remembering to take study pills or poor tolerance of study pills) were noted, these concerns were evaluated and addressed during participant contacts by trained staff and followed-up appropriately.

Symptom Management

Participants were advised on self-care strategies for managing symptoms, such as constipation or bloating. In addition, Clinical Center staff were provided with specific guidelines for temporary "step-down" of study pills (e.g., to one pill a day) in the event that participants were experiencing symptoms or difficulties with taking their study pills. There were no protocol-mandated reasons for unblinding CaD participants' treatment arm. In the unusual event that unblinding was carried out, no clinic staff other than the principal investigator or consulting physician were unblinded to treatment arm.

Protocol-Mandated Reasons for Discontinuing Study Pills

CaD study pills were discontinued, without unblinding treatment arm, for participants who developed certain health conditions (e.g., hypercalcemia, renal calculi, need for hemodialysis) or began taking certain prescription medications (e.g., calcitriol).